AUG 11 1999

NDA 16-295/S-026

Bristol-Myers Squibb Company
P.O. Box 4000
Princeton, NJ 08543-4000

Attention: Joseph A. Linkewich, Pharm.D.
Director, U.S. Regulatory Liaison
Worldwide Regulatory Affairs

Dear Dr. Linkewich:

Please refer to your supplemental new drug application dated November 21, 1996, received November 25, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrea (hydroxyurea capsules,USP).

We acknowledge receipt of your submissions dated October 20, 1997 and November 11, 1997.

This supplemental new drug application provides for the following: revisions in response to the FDA letter dated September 24, 1996 [1) The second sentence in the first paragraph of the **DOSAGE AND ADMINISTRATION** section now reflects the correct number of references. 2) In the **REFERENCES** section, reference item #2 is updated as follows: "2. AMA Council Report:Guidelines for Handling Parental Antineoplastics, JAMA 1985; 253(11): 1590-1592."]; text changes to satisfy the Pediatric Use Rule in the Federal Register Notice dated December 13, 1994; safety updates; revision of obsolete medical text; and editorial changes.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted labeling (package insert submitted November 21, 1996) with the revisions listed below. Accordingly, the supplemental application is approved effective on the date of this letter. However, the following revisions should be included in the final printed labeling.

1. The pregnancy category statement must be revised to be Pregnancy Category D. Revise this subsection in the **PRECAUTIONS** section to: **Pregnancy** Pregnancy Category D. (See **WARNINGS**.)

2. Add the following statement at the beginning of the **Drug Intera**ctions subsection in the **PRECAUTIONS** section: "Prospective studies on the potential for hydroxyurea to interact with other drugs have not been performed."

3. In the first paragraph of the **ADVERSE REACTIONS** section, delete the word "rarely" from the following statement: "Skin cancer has been reported rarely.'

4. In the **WARNING** section, add the **Carcinogenesis and Mutagenesis** subsection and the **Pregnancy** subsection as it appears in the approved DROXIA label.

5. In the **PRECAUTIONS** section, add the **Carcinogenesis, Mutagenesis, and Impairment of Fertility** subsection as it appears in the approved DROXIA label minus the statement "See **WARNINGS** and Boxed **WARNING** for Carcinogenesis and Mutagenesis information."

However, we prefer that you not submit FPL for this labeling until it has been updated and revised to reflect formatting and relevant content of the currently approved DROXIA label. Please update and revise as soon as possible and request an "Expedited Review" of this supplemental application with FPL.

If you proceed with FPL for this supplemental application, S-026, please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 16-295/S-026." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MED WATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Leslie Vaccari, Project Manager, at (301) 594-5778.

Sincerely,

Robert L. Justice, M.D.
Acting Division Director
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research